Management of acute limb ischemia related to underlying pheochromocytoma

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ABSTRACT

Acute limb ischemia (ALI) related to pheochromocytoma is rare. We describe a 69-year-old woman who presented with ALI due to a thromboembolic phenomenon from new-onset atrial fibrillation that was successfully treated with intra-arterial catheter-directed lysis and systemic anticoagulation. Further workup revealed a left adrenal mass and biochemical test results consistent with pheochromocytoma. The patient underwent a retroperitoneoscopic converted to open left adrenalectomy, splenectomy, and distal pancreatectomy because of severe inflammation in the retroperitoneum, probably from an adrenal or subcapsular renal hematoma secondary to systemic anticoagulation. Interval imaging before adrenalectomy for pheochromocytoma should be considered after thrombolysis and anticoagulation for ALI. (J Vasc Surg Cases and Innovative Techniques 2020;6:272-6.)

Keywords: Acute limb ischemia; Pheochromocytoma; Lysis; Hemorrhage

Pheochromocytomas are rare catecholamine-secreting tumors that classically present with paroxysmal hypertension, headaches, and diaphoresis. In rare instances, pheochromocytomas have been associated with acute limb ischemia (ALI). Atrial fibrillation (AF) is a known manifestation of pheochromocytoma and the most common cause of ALI due to thromboembolism.[1]

Treatment options for ALI include an open surgical approach and catheter-directed thrombolysis (CDT). Several trials have demonstrated the efficacy of CDT. However, hemorrhage after CDT is a major complication.[2-4] In this report, we describe a patient presenting with ALI from thromboembolism secondary to AF due to an underlying pheochromocytoma. We examine the treatment options of ALI and give consideration to the risks of thrombolytic therapy and anticoagulation before adrenalectomy. The patient provided consent for the publication of this report.

CASE REPORT

Initial presentation. A 69-year-old woman with no previous cardiac history presented to the emergency department with a chief complaint of dyspnea and left foot numbness and cramping. She also reported a several-week history of dizziness, lightheadedness, and worsening anxiety. She was initially in sinus rhythm and hypertensive to 200/150 mm Hg but was found to be in AF with rapid ventricular response to 190 beats/min and hypotensive to 77/27 mm Hg 30 minutes later.

Physical examination revealed a confused woman with dilated and reactive pupils and a cool left foot with pallor, diminished

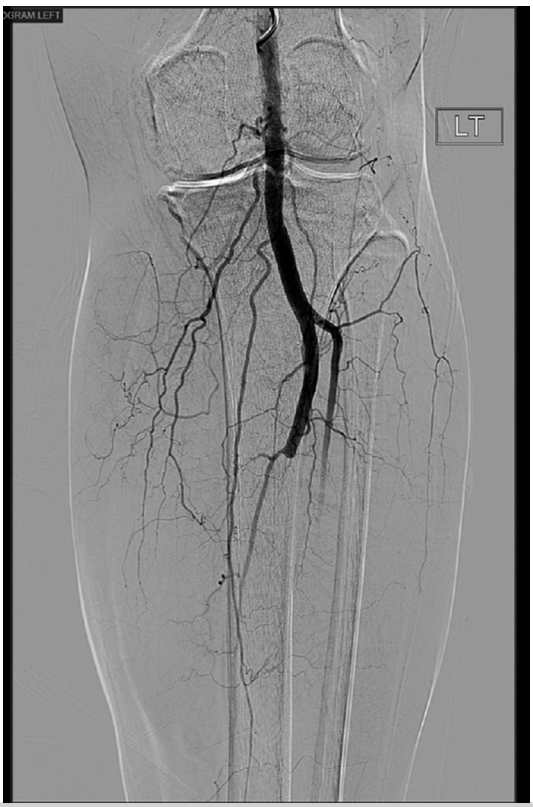

Fig 1. First angiogram demonstrating thromboembolic occlusion at the level of the left tibioperoneal trunk and left anterior tibial artery.

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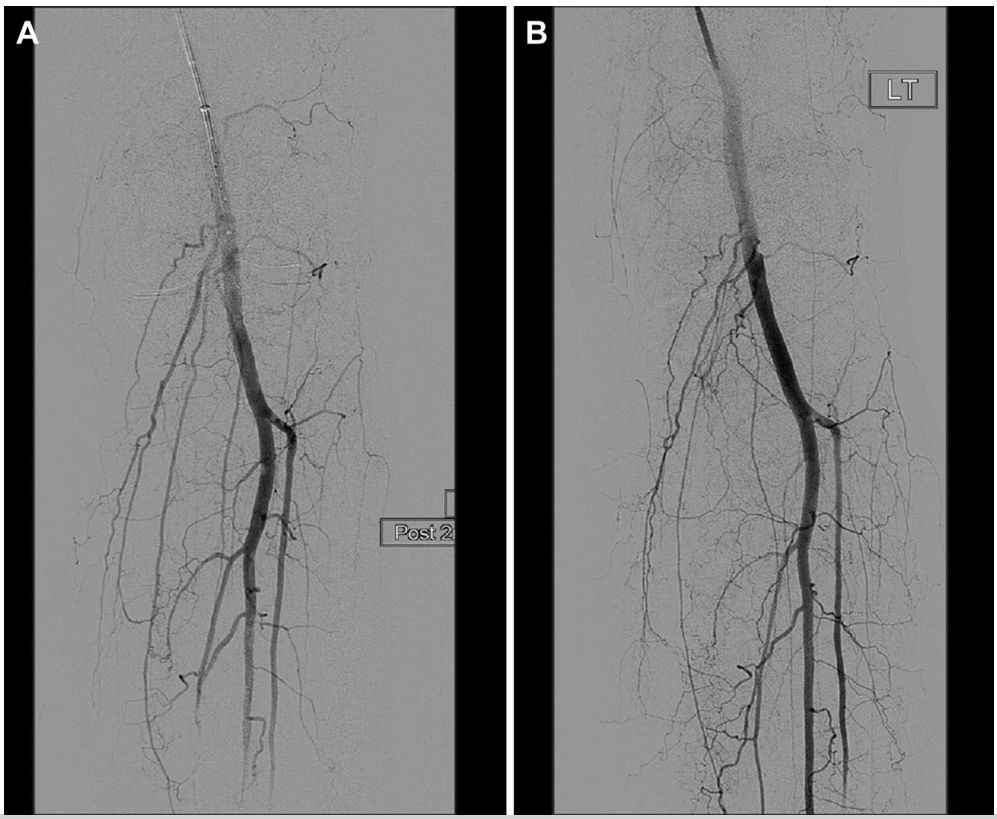

Fig 2. A, Interval angiogram demonstrating successful clot lysis but with evidence of microembolic showering distally. **B,** Final angiogram demonstrating restored flow.

sensation of the digits, moderate tenderness to the distal foot, and no appreciable capillary refill. There were no palpable pulses or Doppler signals distally. Laboratory findings included a white blood cell count of 23,300/μL (normal range, 4160-9950/μL), cardiac troponin I level of 0.15 ng/mL (normal, <0.1 ng/mL), brain natriuretic peptide level of 515 pg/mL (normal, <100 pg/mL), acute kidney injury with a creatinine level of 1.28 mg/dL (patient's baseline, 0.84 mg/dL 2 weeks earlier), lactate level of 7.77 mmol/L (normal, <2.775 mmol/L), and creatine kinase concentration of 101 U/L (normal, 38-282 U/L).

Computed tomography (CT) angiography of the abdomen, pelvis, and runoff through the lower extremities revealed a left adrenal lesion and an abrupt loss of opacification at the mid-distal level of the left anterior tibial artery, minimal short-segment reconstitution of the left peroneal artery at the mid-distal leg with no flow seen proximally or distally, and a diminutive left posterior tibial artery that was unopacified in the mid-distal leg. A 5000-unit heparin bolus was administered. Given the pattern of embolic phenomenon on CT, the absence of tenderness or symptoms proximal to the foot, and hemodynamic instability with large fluctuations in heart rate and blood pressure, we elected to forgo an open embolectomy and to proceed with angiography and CDT. Angiography revealed an abrupt cutoff of the distal tibioperoneal trunk just above the bifurcation to the peroneal and posterior tibial arteries. The anterior tibial artery was patent to the midcalf but demonstrated sluggish flow distally (Fig 1). An intra-arterial lysis catheter was placed across the tibioperoneal occlusion with tissue plasminogen activator (tPA) infusion at 0.5 mg/h and 500 units/h of heparin through the side arm of the sheath. The catheter became dislodged several hours after the procedure because of the patient's discomfort and altered mental status. Angiography was repeated, and the lysis catheter was replaced; tPA infusion was increased to 1 mg/h. The patient was intubated and sedated to prevent further dislodgment. Subsequent angiograms over the next 2 days revealed successful clot lysis but with evidence of microembolic showering distally (Fig 2). Eventually, there was a return of distal pulses and complete return of motor and sensory function. Transthoracic echocardiography did not reveal intracardiac thrombus or evidence of significant cardiomyopathy, and the results of a hypercoagulable workup were negative.

There was high suspicion for an underlying pheochromocytoma given her presenting symptoms, paroxysmal AF, refractory and labile hypertension, and presence of a left adrenal mass on initial CT imaging. A dedicated adrenal protocol CT redemonstrated a 3.7- × 3.3-cm mass of the left adrenal gland with an absolute washout (61%; Fig 3, *A-C*). Also noted was a 3.2-cm amorphous mass in the left ventral abdominal cavity not seen on CT 4 days earlier that was concerning for hematoma (Fig 3, *D*). A full metabolic workup was obtained (Table). Urine and plasma metanephrine and normetanephrine were

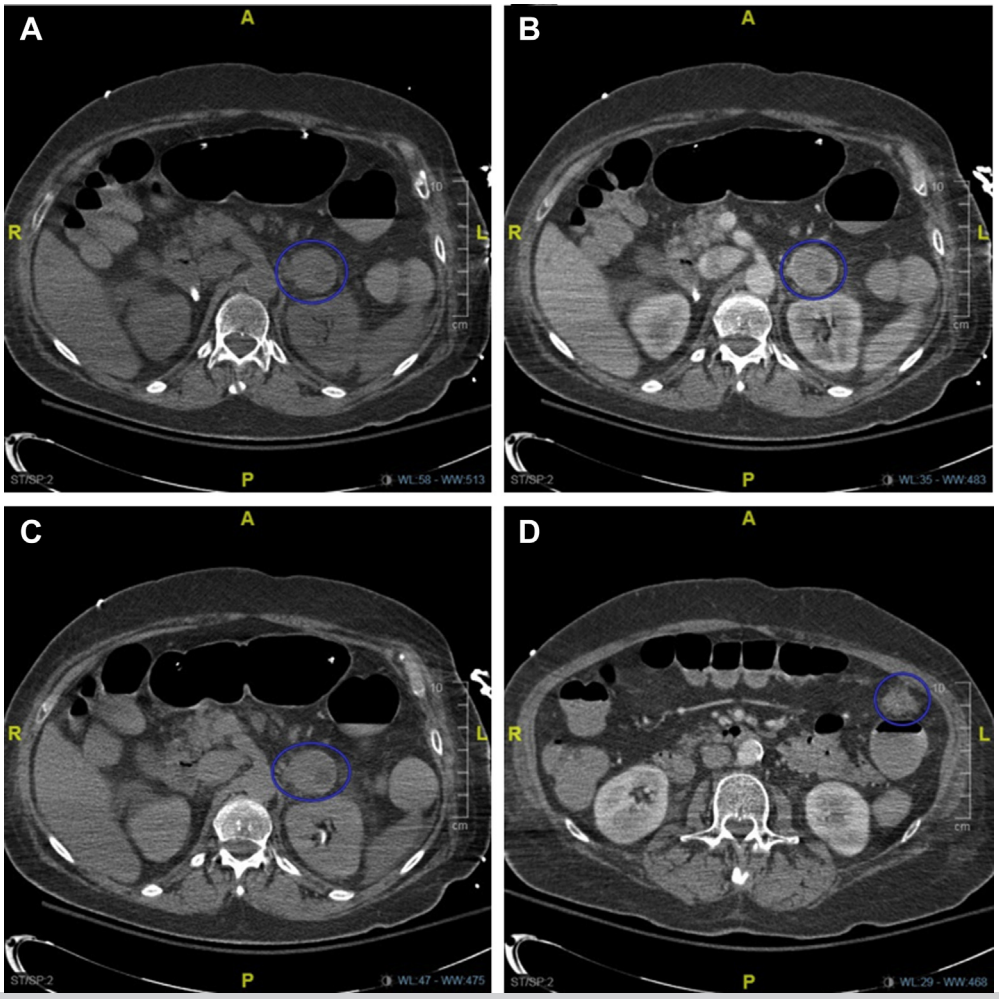

Fig 3. Computed tomography (CT) of left adrenal pheochromocytoma and intraperitoneal hematoma. **A,** Non-contrast-enhanced phase with pheochromocytoma *circled in blue*. **B,** Venous phase with pheochromocytoma *circled in blue*. **C,** Delayed phase with pheochromocytoma *circled in blue*. **D,** Intraperitoneal hematoma *circled in blue*.

markedly elevated, confirming the diagnosis of pheochromocytoma. Urine cortisol was elevated but attributed to a stress response. The patient was subsequently stabilized with a selective alpha blocker (prazosin) and discharged in normal sinus rhythm on doxazosin, amiodarone, metoprolol, diltiazem, and apixaban.

Adrenalectomy. After adequate titration of the alpha blockade, the patient was taken to the operating room for left adrenalectomy 7 weeks after the initial admission, with apixaban held perioperatively. A minimally invasive retroperitoneoscopic approach was attempted. However, severe perinephric inflammation was encountered, suggesting that a hemorrhagic event occurred in the interval period. During the course of dissection, major venous bleeding was encountered, presumably from the splenic vein, which required several maneuvers to control: conversion to an open retroperitoneal approach with partial twelfth rib resection for better exposure and, ultimately, a laparotomy with splenectomy and distal pancreatectomy because of ongoing hemorrhage and severe retroperitoneal inflammation. The adrenal gland was eventually identified and resected. Final pathologic examination revealed a 4.2-cm pheochromocytoma with central hematoma and coagulative necrosis. The patient recovered from surgery and was discharged on postoperative day 10.

DISCUSSION

This case demonstrates a unique presentation of a pheochromocytoma. Here we describe ALI due to thromboembolism in the setting of new-onset AF secondary to an underlying pheochromocytoma. ALI has been described as a manifestation of these tumors in rare instances.[5-7] Approximately 30 cases of thrombus related to pheochromocytoma have been reported in the literature.[6,8] Kaiser et al[6] reported that the first major thrombotic event in 78% of these patients occurred around the time of tumor discovery. However, the majority of these cases involved venous thromboses,

Table. Biochemical results for workup of pheochromocytoma

Laboratory test	Value	Normal range
Renin activity	4.2 ng/mL/h	0.2-1.6 (supine) 0.5-4.0 (upright)
ACTH	30 pg/mL	4-48
Aldosterone	3.9 ng/dL	≤16
Renin/aldosterone ratio	1:1.07	
Plasma metanephrine, free	8.6 nmol/L	0.00-0.49
Plasma normetanephrine, free	6.84 nmol/L	0.00-0.89
Urine metanephrine (24-hour)	6262 mg/dL	39-143
Urine normetanephrine (24-hour)	2200 mg/dL	109-393
Urine 5-HIAA/creatinine ratio (24-hour)	4 mg/g creatinine	0-14
Urine cortisol/creatinine ratio	637.68 μg/g creatinine	<24
DHEA-S	1190 ng/mL	400-3600
TSH	0.19 mcIU/mL	0.3-4.7
T_3, total	53 ng/dL	85-185
T_4, free	1.1 ng/dL	0.8-1.7

ACTH, Adrenocorticotropic hormone; *5-HIAA,* 5-hydroxyindoleacetic acid; *DHEA-S,* dehydroepiandrosterone sulfate; *TSH,* thyroid-stimulating hormone; *T_3,* triiodothyronine; *T_4,* thyroxine.

particularly of the inferior vena cava, because of tumor compression or extension to the inferior vena cava or other nearby veins. In the general population, cardiogenic emboli contribute to 80% of embolic arterial occlusions.[1] In the case of pheochromocytoma, intracardiac thrombus is a leading cause of ALI and is usually secondary to cardiomyopathy. However, our patient had appropriate wall motion and ejection fraction and no evidence of intracardiac thrombus on echocardiography.

Treatment of ALI includes an open surgical approach and CDT. Early trials demonstrated successful CDT in 70% of ALI cases.[2] However, major bleeding was significantly higher in the thrombolysis group and occurred in approximately 8% of cases within 30 days.[3] A large portion of the study population had pre-existing peripheral vascular disease or presented with graft occlusion. As such, the majority of cases were ALI secondary to thrombosis rather than embolic phenomenon. A retrospective cohort study of native artery ALI found that CDT was an effective therapeutic option with mortality and amputation-free survival similar to published data. However, hemorrhage remained a major complication.[4]

Recognizing our patient's hemodynamic instability and symptoms isolated to the foot, the decision was made to proceed with thrombolysis over surgical thromboembolectomy. Although CDT with systemic anticoagulation was successful, the initial intra-arterial lysis catheter became dislodged, which probably resulted in systemic circulation of tPA, although for a short time. Spontaneous hemorrhage of adrenal pheochromocytomas is rare but can be catastrophic.[9] At least one case of massive hemorrhage of a pheochromocytoma occurred after systemic thrombolytic therapy for an acute myocardial infarction and resulted in death.[9] In our patient, the dedicated adrenal CT during the initial hospitalization demonstrated an intra-abdominal lesion consistent with hematoma, but this lesion was not near the adrenal gland or other retroperitoneal structures. Although our patient did not develop overt signs or symptoms of intra-abdominal hemorrhage, repeated imaging before adrenalectomy should have been considered, given the high rate of hemorrhage in patients treated with thrombolysis and anticoagulation as well as the increased risk of tumor hemorrhage with pheochromocytoma. Additional imaging would have identified the extent of hematoma and could have guided the operative approach or the decision to delay surgery.

CONCLUSIONS

This case highlights a diagnosis of ALI due to thromboembolic phenomenon in the setting of AF, leading to the diagnosis of pheochromocytoma. Prompt diagnosis and therapeutic intervention are critical for limb preservation. A viable option for treatment of ALI due to thromboembolism is CDT and anticoagulation. Interval imaging closer to the date of adrenalectomy for pheochromocytoma is recommended to identify evidence of bleeding or hematoma that might affect the operation.

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